REMARKS

Interview Summary

Pursuant to 37 CFR §1.133(b), Applicants acknowledge with appreciation the personal interview with the Examiner on August 6, 2008, during which the following outstanding issues were discussed. In particular, Applicants discussed the rejection based on obviousness over WO 01/85798 in view of US 5,869,057. Applicants agreed to submit their arguments and supporting references in writing regarding the patentability of the claimed molecular conjugates.

Claim Amendments

Claims 33-36, 39-44, 47-52, and 55-59 were pending. Claims 33-35, 49, 50, 52, and 59 have been amended.

Specifically, claims 33-35, 49, 50, 52, and 59 have been amended to specify that the antigen is βhCG.

The foregoing claim amendments should in no way be construed as acquiescence to any of the Examiner's rejections and were made solely to expedite prosecution of the application. Applicants reserve the right to pursue claims to the canceled subject matter, or any subject matter which they are entitled to claim, in this or a separate application. No new matter has been added.

Rejection of Claims 33-36, 39-44, 47-52, and 55-59 Under 35 U.S.C. §103(a)

Claims 33-36, 39-44, 47-52, and 55-59 are rejected as being unpatentable over WO 01/85798 in view of US 5,869,057. The Examiner acknowledges that WO 01/85798 "does not teach the use of βhCG as an antigen." However, the Examiner relies on US 5,869,057 as teaching "the use of βhCG as an antigen . . . [as well as its use in] immunization [and] antimetastasis treatment."

Applicants respectfully traverse this rejection. The '057 patent teaches the use of the antigen, β human chorionic gonadotropin (βhCG), for use as a vaccine. However, this reference fails to teach the claimed methods which employ a conjugate of βhCG and an antibody against MMR to form a molecular conjugate which directly targets the human MMR on APCs and induces an immune response mediated by both $CD4^+$ and $CD8^+$ T cells. Nor would there have been any motivation or reasonable expectation of success in achieving the claimed method, based on what was known in the art concerning βhCG.

Specifically, the '057 patent teaches linking a microbial (non-self) gene product (*e.g.*, a prokaryotic helper T cell epitope, such as heat-labile entertoxin B subunit (LTB)) to a ***"self" gene product*** (*e.g.*, a βhCG epitope) for the production of an immune response to the self protein. According to the '057 patent, the use of "foreign (non-self) T cell epitopes and the natural adjuvant properties of microbial gene products" is required to produce a therapeutically acceptable vaccine (see, *e.g.*, col. 11, lines 19-23). Such adjuvants "***must be included in the vaccine formulation in order for processing and presentation of T cell epitopes by specialized antigen presenting cells such as macrophages and dendritic epidermal cells to occur***" (col. 11, lines 3-7) (emphasis added). Therefore, based on the teachings of the '057 patent, one of ordinary skill would not have been motivated to have linked βhCG with an antibody to generate an immune response, as claimed, since it was well known that antibodies are not microbial gene products, and do not have microbial adjuvant properties, such as helper T cell epitopes.

Moreover, at the time the present application was filed, human βhCG antigen was well known to be "self-tolerant." Accordingly, to break this tolerance, it was understood by those skilled in the art that a βhCG-based vaccine ***must*** include a potent carrier, as well as combining it with an adjuvant. See, for example, the '057 patent, cited above, as well as Lund and Delves (1998), Reviews of Reproduction 3:71-76, which states that:

> [t]he glycoprotein hormones are 'self' antigens. Although normally expressed only during pregnancy, it appears that hCG is very effective at establishing immunological tolerance. There are hardly any reports of circulating autoantibodies to the hormone being detected in humans, even in patients with a history of recurrent spontaneous abortion (Tulppala *et al.*, 1992). However, it is also clear that this tolerance is not absolute, because when it is administered coupled to a potent carrier and in the presence of adjuvant, hCG can break tolerance and elicit an immune response.

(paragraph spanning pages 74-75) enclosed as Appendix A. Further evidence that the prior art believed the only relevant form of βhCG vaccine was one which was linked to an immune carrier is provided by Triozzi *et al.* This reference describes conjugates of βhCG-CT coupled to diphtheria toxoid and combined with the adjuvant, muramyl dipeptide and a vehicle, squalene/mannide monooleate (Ann NY Acad Sci (1993); enclosed as Appendix B).

In contrast, Applicants developed an effective method for generating an immune response against βhCG, which does not require (but can include) foreign (non-self) T cell epitopes and adjuvants, as taught by the prior art. Moreover, Applicants were the first to show that by using a molecular conjugate of βhCG linked to an anti-MMR-antibody, the presently

claimed methods were capable of inducing a cytotoxic T cell response mediated by both $CD4^+$ and $CD8^+$ T cells against βhCG. Specifically, βhCG is targeted to the MMR and processed through both MHC class I and class II pathways. Thus, antigen-specific CTLs (*e.g.*, $CD8^+$ T cells) are activated, as well as other important effector T cells, including helper T cells (*e.g.*, $CD4^+$ T cells).

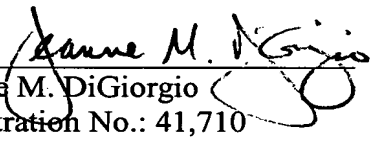
Based on at least the foregoing, the claimed molecular conjugates are patentable.

SUMMARY

Based on the foregoing amendments and arguments, reconsideration and withdrawal of all the rejections and allowance of this application with all pending claims are respectfully requested. If a telephone conversation with Applicants' Attorney would expedite the prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 227-7400.

Dated: September 3, 2008

Respectfully submitted,

By 

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